UNITED STATE DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/684,794	10/10/00	YANG	R

HM22/0504

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EXAMINER	
HUYNH,P	
ART UNIT	PAPER NUMBER
1644	6

DATE MAILED:
05/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/684,794	YANG ET AL.	
	Examin r	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *8-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

1. Applicants' preliminary amendment, filed 4/23/01 (Paper No. 5) is acknowledged. The specification has been amended.

2. Applicants' election of Group I, claims 1-7 (Paper No. 4) is acknowledged. Because applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
Claims 1-12 are pending.
Claims 1-7 are being acted upon in this Office Action.
Claims 8-12 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. This application is required to be review and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Appropriate correction is required in the specification, See, e.g. "The best concentrations of NaCl in phosphate **butter** eluants for DEAE-Sephadex A50 and Sephadex G200 are **0.07Mand 0, 1M**, respectively" on page 2 line 24. It should have been "The best concentrations of NaCl in phosphate **buffer** eluants for DEAE-Saphadex A50 and Sephadex G200 **are 0.07M and 0.1M**, respectively". Also see page 3 line 3 "90%and 10%", page 3 line 21 "I:51", page 4 line 24 "2x10 /ml", page 5 line 1 "1.0ml 91x10 /ml)", page 5, line 20 "2x10°C", page 5 line 21 "2x10/ml", page 5 line 22 "2x10 /ml", page 5 line 26 "1x10 /ml".

4. Claims 1, 3-5 are objected to because it is unclear what applicant meant by "extracting **clued** IgY by water dilution" as recited in claim 3. Do applicants meant "crude"? Also, Claims 1, 3-5 recite "NaC1" instead of "NaCl" wherein the "l" appears to be numeral number 1. The word "streptococcus" is recited twice in a row in claim 1. Appropriate correction is required.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "**including....which are**" as recited in claim 1 is indefinite because the metes and bounds of the claim as written is unclear. It is suggested that Applicants amend the claim using functional language. For example, A preparation method of ...comprising ..."

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: recovering said IgY immunoglobulin.

Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee *et al.* (US Pat No. 5,367,054, Nov 1994; PTO 892) and or Akita *et al* (J. of Food Science: 57(3): 629-634; PTO 892) in view of Hatta *et al* (Caries Res 31(4): 268-74, 1997, PTO 892) or Hamada et al (Microbiol Immunol 22(6): 301-314, 1978; PTO 892) or Natarajan et al (Dev Comp Immunol 8(4): 845-54, 1984; PTO 892).

Lee *et al* teach a method of preparing egg immunoglobulin Y (IgY) against *Streptococcus mutans* (See column 8, line 26, in particular) wherein the method steps comprising immunizing hens with bacterial antigens of interest i.e., *Streptococcus mutans*, extracting IgY by water dilution, follow by anion exchange (DEAE-Sephadex) column chromatography. The method consists of the following steps (See column 5, line 25; column 8, line 8 in particular). First, hyper-immunized the bird (chicken or duck) with the antigens of interest including Streptococcus mutans (See column 8, line 26, in particular). Second, the IgY immunoglobulin of the egg yolk is initially extracted by water dilution with 4-6 fold of distilled water (See entire document, column 2, line 24, in particular), the pH of the water soluble fraction is then adjusted to about 4-6 or near pH 7.0 (column 5, line 49; column 5, line 66; column 10 line 68, in particular), and let the water soluble solution stand at 3-4 °C (See column 2, line 24, in particular), and centrifuging at high speed at about 2500-30,000 rpm (See column 5, line 44, in particular). After water extraction, the aqueous phase is subjected to a combination of size exclusion through a 30K or 100K cut off filter from Amicon or gel filtration and anion exchange DEAE (diethylaminoethyl) Sephadex chromatography (See entire document, column 10 line 69 bridging column 11; column 6, line 15; column 6 line 55, Fig 1, in particular). For ion exchange chromatography, the column matrix that is suitable for large scale IgY purification includes DEAE (diethylaminoethyl)-Sepharose or DEAE-Sephadex wherein the IgY is eluted with DEAE ion exchange buffer (eluant) which is a sodium phosphate buffer containing about 0.01-0.4M NaCl as the final salt concentration (See entire document, column 5 line 49, in particular). Other suitable anion-exchange chromatography materials as well as the selection of using these materials are known to those ordinary skilled in the art (See column 6, line 55, in particular).

The claimed invention differs from Lee *et al* by preparing IgY against dental carries using *streptococcus mutans* serotype c and d. The IgY immunoglobulins were separated by size using gel filtration on a Sephadex G200 column with an eluant phosphate buffer containing 0.05-0.2M of NaCl and preferably containing 0.1M of NaCl salt concentration. In the instant case, the high molecular weight proteins are eluted first and the various immunoglobulins are then eluted

according to molecular size in decreasing order with a molecular weight cut off between 5000 to 6000 Dalton.

However, Akita *et al* teach a preparation method of extracting egg IgY immunoglobulin by water dilution with six-fold of water, adjusting the pH 5.0 to 5.2, let it stands for at least 2 hr before high speed centrifugation (See entire document, page 629 Materials and Methods) to yield 100mg pure IgY per egg by a combination of ultrafiltration, gel filtration with Sephacryl S-200 using 0.1M phosphate buffer at pH 7.0 and DEAE-Sephacel anion exchange chromatography equilibrate with the appropriate starting buffer (See entire document, Materials and Methods, page 630, in particular) wherein the choice of column depends on the amount of IgY to be purified. Furthermore, Akita et al teach that the optimal dilution of egg yolk with six-fold of water at a pH 5.0 and incubation time of 6 hour at 4 °C gave an IgY recovery of 93-96% (See page 632, right column second paragraph). The reference also recommended that the use of gel filtration or anion exchange as the final steps should be most efficient. The advantages of this protocol are that the procedure is simple, rapid and produces high yields of active IgY (See page 633, right column last paragraph, in particular).

Hatta *et al* teach a method preparation against dental carries in humans by mouth rinse containing *Streptococcus mutants* serotype c specific Egg IgY immunoglobulin (See entire document, page 269 Materials and Methods, in particular). Furthermore, Hatta *et al* teach a method of purifying IgY by anion exchange column chromatography using DEAE-Sephacel from Pharmacia.

Hamada *et al* teach clinical strains of Streptococcus mutans isolated from Japanese children with dental caries (See entire document, Table 5 in particular). All the clinical isolates (7 strains) of S. mutans, belonging to serotypes c, d, e, and f develop plaque on the molar teeth and induced dental caries in SD rat (See page 306, in particular). In particular, serotype d strain preferentially developed smooth surface caries as well as caries of fissure origin (See page 312, first paragraph).

Natarjan et al teach the method of purifying various classes of immunoglobulins using a combination of ion-exchange chromatography on DEAE-cellulose and gel filtration on Sephadex G-200 (See entire document, abstract, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to prepare egg IgY immunoglobulin against dental caries by immunizing the bird with the antigen specific for serotype c and d of *Streptococcus mutans* as

taught by Hamada *et al* by substitute the antigen taught by Lee and purifying large quantity of IgY using a combination of ion-exchange chromatography and gel filtration on Sephadex G-200 as taught by Lee, Hatta and Natarajan. Since the use of DEAE column and gel filtration chromatography was well within the purview of an ordinary artisan at the time the invention was made, the method steps lends no patentable weight to the claimed invention. One having ordinary skill in the art would have been motivated to prepare immunoglobulin Y (IgY) against dental caries bacteria from *streptococcus mutans* antigens type c and d because they are the principal etiological agents of dental caries in humans and IgY specific for *streptococcus mutans* has been demonstrated to be effective in protecting the host against dental caries. The advantage of IgY preparation is that the preparation method does not require the bleeding the animals for antiserum production as taught by Hatta (See abstract and page 269 left column 1st paragraph). Furthermore, anion exchange coupling with gel filtration size exchange chromatography has been considered a useful method for purifying egg immunoglobulin IgY in large quantity (Lee, Hatta and Natarajan) wherein the purified IgY can be used for pharmaceutical purposes including a preparation against dental caries as taught by Hatta *et al*.

10. Claims 2, and 5-7 are free of prior art; however, no claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

12. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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